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10/566,911	02/03/2006	Bum Tae Kim	DE1672	1133

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EXAMINER	
RICCI, CRAIG D	
ART UNIT	PAPER NUMBER
1614	
MAIL DATE	DELIVERY MODE
01/07/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/566,911	KIM ET AL.	
	Examiner	Art Unit	
	CRAIG RICCI	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 October 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

2. Applicants' arguments, filed 09/25/2008, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 103

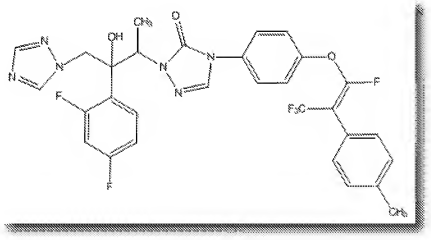
3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

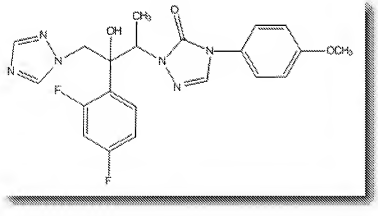
5. **Claims1 and 3 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Itoh et al* (US 5,371,101) in view of *Kim et al* (US 6,552,080).**

6. Instant claim 1 is drawn to compounds of formula (I) which encompass the following compound

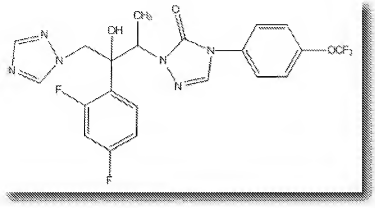


(Table V, Example 90) and which are alleged antifungal compounds.

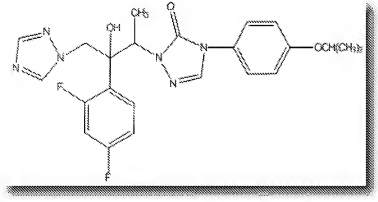
7. *Itoh et al* teach structurally and functionally related compounds. Specifically, *Itoh et al* teach the following antifungal compounds:



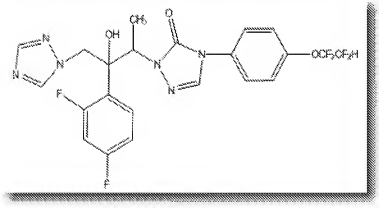
(Column 59, Table 9, No. 8)



(Column 59, Table 9, No. 12)

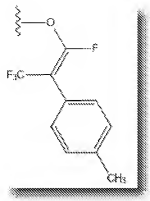


(Column 61, Table 12, No. 32)

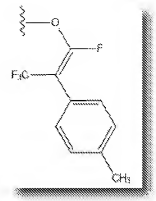
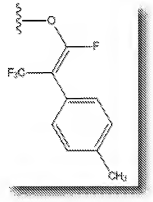


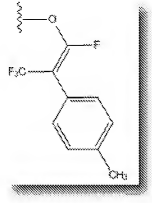
(Column 61, Table 13, No. 34)

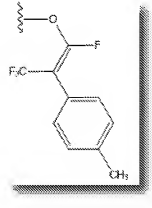
Although *Itoh et al* do not teach the compound recited by instant claim 1, it is noted that the core structure taught by *Itoh et al* is identical to the core structure of the compound recited by instant claim 1 and, furthermore, that the compound of instant claim 1 differs

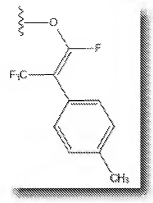
from *Itoh et al* only in the substitution of phenol with  (in the instant compound) as opposed to, for example, O-CF_3 (In *Itoh et al*). It would have been obvious to a person of ordinary skill in the art at the time the invention was made to include this moiety in the compound taught by *Itoh et al* for the following reasons:

8. **FIRST**, *Itoh et al* disclose several compounds containing the same core structure as the compounds of instant claim 1 which differ only in the modification at phenol and *Itoh et al* teach that these compounds can be modified at phenol. For example, in the above discussed examples disclosed by *Itoh et al*, the reference teaches modifications at phenol such as $-OCH_3$, $-OCF_3$, and $-O(CH)(CH_3)_2$ etc. Accordingly, it would have been obvious to a person of ordinary skill in the art to envisage modification of the compound taught by *Itoh et al* and, furthermore, it would have been obvious to a person of ordinary skill in the art to envisage modifying the compound taught by *Itoh et al* at that specific position; namely, phenol.

9. **SECOND**, *Kim et al* teach the group represented by  in fungicidal compounds (For example, Column 41, Example No. 105). More specifically, *Kim et al* teach "a fungicidal compound... having a fluorovinyl... moiety... useful for protecting crops from fungal diseases" (abstract). Accordingly, one of ordinary skill in the art at the time the invention was made would have recognized that compounds containing the group represented by  have fungicidal activity.

10. **THIRD**, *Kim et al* specifically provide the motivation to include the group represented by  in fungicidal compounds. Specifically, *Kim et al* teach that "the compounds of the present invention have a broad fungicidal activity spectrum against the target fungi when compared with the control compounds such as ORIBRIGHT and FENARIMOL" (Column 57, Lines 53-57). Notably, although ORIBRIGHT™ and FENARIMOL™ share some structural similarities with the compound disclosed by *Kim et all*, neither ORIBRIGHT™ nor FENARIMOL™ contain a fluorovinyl moiety. Accordingly, one of ordinary skill in the art at the time the invention was made would have recognized a motivation to include the moiety in compounds having antifungal activity.

11. **And FOURTH**, *Kim et al* teach that it is routine to react phenol with the group represented by  to generate compounds. Specifically, *Kim et al*

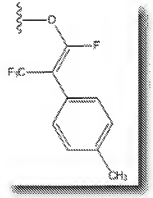


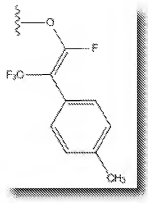
teach the reaction of the group represented by with phenol in Reaction Scheme G (Column 12, Lines 50-65). As disclosed by *Kim et al*, the reaction as shown in Reaction Scheme G is carried out "according to a conventional method" (Column 12, Lines 45-49). Accordingly, one of ordinary skill in the art at the time the invention was made would have known to react the moiety at phenol.

12. Thus, based on *Kim et al* - which teach that compounds containing a fluorovinyl moiety exhibit enhanced fungicidal activity compared with compounds that lack the moiety - it would have been obvious to one of ordinary skill in the art at the time the invention was made to include a fluorovinyl moiety into the invention taught by *Itoh et al*, a known fungicidal, in an effort to enhance the fungicidal activity. Furthermore, it would have been obvious to a person of ordinary skill in the art to include the moiety at the phenol position in *Itoh et al* to generate a compound encompassed by instant claim 1 since *Itoh et al* teach that the phenol position is capable of being modified and additionally because *Kim et al* specifically teach the addition of the moiety at phenol. In light of the foregoing, claim 1 is obvious.

13. Instant claim 3 is drawn to "a fungicidal composition comprising the compound according to claim 1 or 3 as an active ingredient and an inert carrier" (claim 3). *Itoh et al*

specifically teach the compound "when it is used as an antifungal agent... is dissolved or dispersed in a suitable liquid carrier or mixed or absorbed with a suitable solid carried" (Column 14, Lines 47-52) and that "examples of the liquid carried used are water..." (Column 14, Line 63). Thus, *Itoh et al* specifically teach the compound which, as discussed above, is obvious in view of *Kim et al*, as an active ingredient with an inert carried in a fungicidal composition. Accordingly, claim 3 is obvious.

14. Applicant's argument that one of ordinary skill in the art would **not** have found it obvious to combine the references of *Itoh et al* and *Kim et al* to modify the core structure of *Itoh* with  as disclosed in *Kim et al* is not found persuasive. Applicant argues that the core structures of *Kim et al* and *Itoh et al* are quite different from each other. Although Applicant is correct that the core structures of *Kim et al* and *Itoh et al* are quite different from each other, the core structure of *Itoh et al* and the **instant invention** are identical, with the only difference being the substitution of



phenol in the compounds taught by *Itoh et al* with in the instant invention. *Kim et al* teaches the above fluorvinyl moiety in compounds having enhanced fungicidal activity over related compounds lacking the fluorovinyl moiety. Thus, the skilled artisan would have been motivated to include the fluorovinyl moiety in other antifungal compounds (such as those taught by *Itoh et al*) in an effort to enhance antifungal activity of such compounds and, in doing so, would have arrived at the instant compounds. Thus, it is irrelevant that the core structures of *Kim et al* and *Itoh et al* are different from each other.

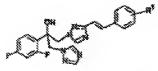
15. Applicant further argues that the purpose of the present invention is to provide a compound having a high anti-fungal activity against a wide spectrum of pathogenic fungi which also exhibits low toxicity. Since the fungicidal compound of *Kim et al* is useful only for treating crops, not humans, Applicant contends it would not have been obvious to modify the teaching of *Itoh et al* with *Kim et al* to arrive at the instant invention. However, Applicant's argument is based on limitations which are not present in the claims. No where in the claims does Applicant recite that the azole derivatives of formula (I) are of low toxicity or useful for humans for oral administration. Accordingly, these limitations are not accorded patentable weight. The skilled artisan would have

been motivated to combine the teachings of *Itoh et al* with *Kim et al* to enhance the fungicidal activity of the compounds taught by *Itoh et al*. Since *Itoh et al* clearly teach that the compounds disclosed can be "used as an antifungal agent for agricultural purposes" (Column 14, Lines 48-49) the skilled artisan would have readily looked to *Kim et al* for guidance.

16. **Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over *Itoh et al* (US 5,371,101) in view of *Kim et al* (US 6,552,080) as applied to claims 1 and 3 above, and in further view of *Boyle et al* (Ann NY Acad Sci 544:86-100, 1988), cited in a previous Office Action.**

17. As discussed above, the compound of formula (I) as recited by claim 1 is obvious under *Itoh et al* in view *of Kim et al*. However, *Itoh et al* in view of *Kim et al* do not teach antifungal compounds containing the non-oxygenated triazole as recited by instant claim 2.

18. *Boyle et al* teach antifungal compounds containing a non-oxygenated triazole attached to the identical core described by the instant application (entire document). More specifically, *Boyle et al* teach, for example, the following compounds with antifungal activity having a non-oxygenated triazole attached to the instant core:



Compound Number	R'	Activity: *C. albicans* in Vitro (μg/ml, IC_{80})	Antifungal Spectrum (μg/ml, MIC) Yeast	Mycelium	Dermatophyte	*C. albicans* in Vivo (mg/kg)	Half-life in Rat (days)
23	4-CN	0.12	100-1.6	0.01	100-1.6	1.0	1
24	4-$CONH_2$	0.53	> 100	0.01	(100)	> 25	
30	4-$CON(Me)CH_2C_6F_5$	0.006	25-6.2	< 0.01	≤ 1.6	10	
20	4-OCF_3	0.05	6.2-1.6	< 0.001	1.6	0.25	6.5
33	4-OCF_2CF_2H	0.006	100-1.6	< 0.01	6.2-1.6	0.25	9
32	4-OCH_2CF_3	0.03	1.6	< 0.01	1.6	0.5	1.5
34	4-$OCH_2CF_2CF_2H$	0.003	6.2-1.6	< 0.01	≤ 1.6	0.25	1
31	4-OCH_2CH_2F	0.003	25-1.6	< 0.001	1.6	25	
21	4-OCH_3	0.001	100-1.6	< 0.01	25-1.6	> 25	

(Page 97, Table 5). Accordingly, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to use compounds having either an oxygenated triazole (as taught by *Itoh et al*) or a non-oxygenated triazole (as taught by *Boyle et al*).

19. Applicant's argument that one of ordinary skill in the art at the time the invention was made would never have utilized the compounds or teachings of *Boyle et al* to modify the primary and secondary references of *Itoh et al* and *Kim et al* is not found persuasive. Applicant argues that the majority of compounds cited in Table 5 above were not considered to be appropriate and efficacious for *in vivo* use. Again, Applicant's argument is based on limitations which are not present in the claims. No where in the claims does Applicant recite that the azole derivatives of formula (I) are for *in vivo* use. Accordingly, these limitations are not accorded patentable weight. Furthermore, *assuming arguendo* that the limitations had been accorded patentable weight, Applicant is directed to Page 98, Paragraph 2 of *Boyle et al*, referring to compound 34 listed on Table 5 above, "ICI 195,739... had a nearly optimal profile of

increased *in vitro* potency, a broad spectrum of activity, an oral activity at 0.50-0.25 mg/kg, and an elimination half-life of 24 hr."

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CRAIG RICCI whose telephone number is (571) 270-5864. The examiner can normally be reached on Monday through Thursday, and every other Friday, 7:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/CRAIG RICCI/
Examiner, Art Unit 1614

/Ardin Marschel/

Supervisory Patent Examiner, Art Unit 1614